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Giant primary malignant mesothelioma of the liver: A case report

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ABSTRACT

INTRODUCTION: Malignant mesothelioma is a rare neoplasm of mesothelial cells arising most frequently in the pleura or peritoneum and less frequently in the liver.
CASE PRESENTATION: We present a case of primary hepatic mesothelioma of 41 year old woman. She had no history of asbestos exposure or cancer. Abdominal computed tomography (CT) showed 21 cm intrahepatic mass in the right lobe with many cystic lesions and few small calcifications. Pathology showed a biphasic cellular pattern. In addition, the tumor cells were positive for Calretinin, Creatine Kinase (CK)5/6, CK7, CKAEI 1/3, Wilms Tumor protein (WT-1), and Vimentin, but were negative for Alpha Feto protein (AFP), Thrombotic Thrombocytopenic Purpura (TTP-1), Anti-Hepatocyte Specific Antigen (HSA), Synaptophysin, CK20, and Homeobox protein (CDx-2).
DISCUSSION: Primary intrahepatic mesothelioma (PIHMM) is not included in the classification of the World Health Organization classification of hepatic tumors. Mesothelial cells are not normally found in the liver, but some reported cases suggest it may grow from the mesothelial cells of the Glisson's capsule.
CONCLUSION: The probability of hepatic mesothelioma should not be ruled out, even in a young woman without a clear history of asbestos exposure.

1. Introduction

Primary malignant mesothelioma of the liver is an extremely rare pathology. It is commonly found in the pleura, peritoneum and pericardium. Mesotheliomas are most commonly associated with exposure to asbestos [1]. Less common etiology includes MC29 avian virus [2]. Epidemiologic data suggests that genetic predisposition might have an essential role in determining the development of mesothelioma since the analysis of pedigrees of families affected by mesotheliomas showed that these mesotheliomas seemed to be inherited in an autosomal dominant pattern [3].

We are reporting a rare case of a primary intrahepatic mesothelioma in a 41-year-old female patient.

2. Case presentation

A 41-year old female patient was referred to our institution with right hypochondriac pain and dizziness for one month. The pain was associated with fatigue, weight loss, periodic low-grade fever and tachycardia. Physical examination revealed a large palpable mass in the right upper abdomen extending to the pelvis. She had no history of prior asbestos exposure, cigarette smoking or alcohol use.

Laboratory examinations revealed anemia with Hb level = 8.4 g/dL (range Female 12.0–16.0), and Hct% = 27% (range Female 37.0–46.0). Liver function tests showed elevated alkaline phosphatase (ALP) = 407 IU/L (range 35–120), gamma-glutamyl transferase (g-GT) = 211 IU/L (range 10–50) and international normalized ratio (INR) = 1.6 (range 0.8–1.1). The rest of the laboratory examinations were within normal ranges. Viral markers related to hepatitis B virus (HBV) and hepatitis C virus (HCV) infection were negative.

Computed tomography scan (CT scan) revealed a mass in the liver measuring 21 × 20 × 15.5 cm occupying the right lobe with multiple cystic lesions and few small calcifications (Figs. 1 and 2). The mass was reaching the periphery of the liver causing capsular indentation on the liver with adjacent perihepatic fluid. There are several arterial feeding collaterals arising from the right hepatic artery. The enlarged liver is compressing the adjacent bowel loops, right kidney, right adrenal, and the inferior vena cava. The portal vein is normal in caliber measuring 11 mm and patent. The pancreas, spleen, adrenals, kidneys and bowel loops are unremarkable.

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Fig. 1. Coronal Computed Tomography scan. The figure shows a coronal CT triple phase scan of the liver displaying a 21 × 20 × 15.5 cm mass occupying the right lobe with multiple cystic lesions and few small calcifications.

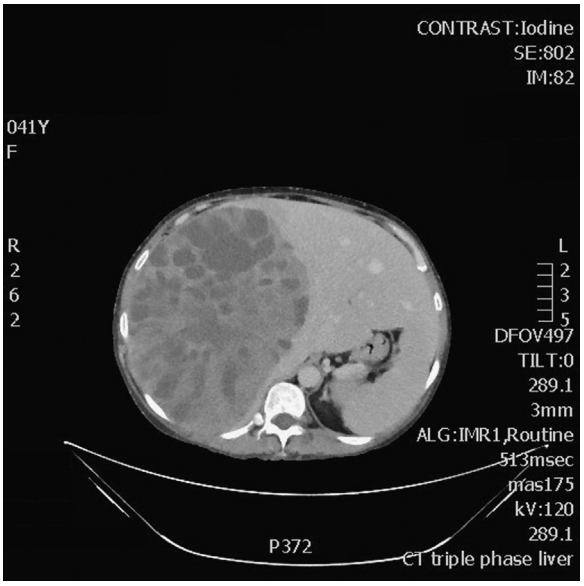

Fig. 2. Transverse Computed Tomography scan. The figure shows a cross-sectional scan of the mass occupying the right lobe of the liver.

Celiac trunk, superior mesenteric artery, and inferior mesenteric artery are patent.

The case was discussed in the Tumor Board, and decision was made to go for surgery. The patient underwent right hepatectomy with cholecystectomy (Fig. 3). She did well postoperatively and was discharged on day 10 post surgery.

Pathology revealed a biphasic cellular pattern. In areas, the epithelioid cells were arranged in gland-like structures and in solid sheets. In other areas, the cells were splindled and embedded in a fibrotic stroma. The cells exhibited mild to moderate cytologic

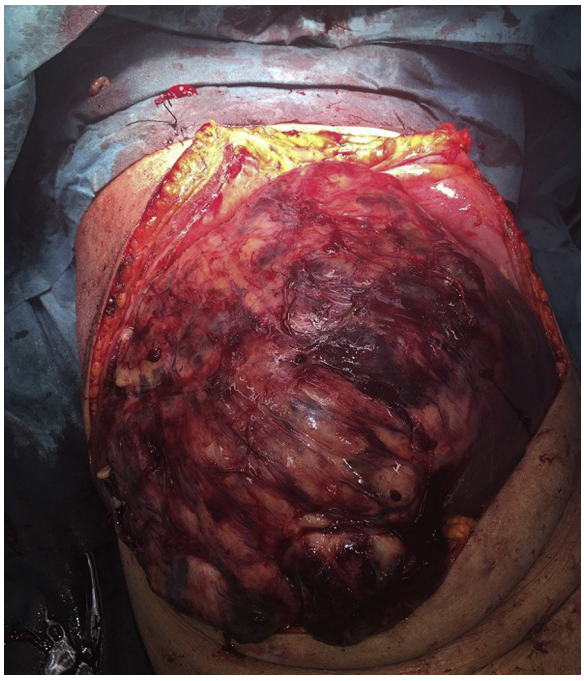

Fig. 3. Mass displaying well-circumscribed heterogeneous lesion. The figure shows a 24 × 20 × 12 cm mass weighing 4.6 kg. It has a multi-cystic and solid tan-yellow soft cut surface.

atypia. Few mitoses and multinucleated giant cells were noted. Extensive areas of necrosis were present. In addition, the gallbladder showed chronic cholecystitis without stones.

Immunohistochemically, tumor cells were positive for Calretinin, CK5/6, CK7, CKAEI 1/3, WT-1, and Vimentin. However, it was negative for AFP, TTP-1, HSA, Synaptophysin, CK20, and CDx-2. These findings were consistent with primary intrahepatic malignant mesothelioma. Surgical margins were free of disease. No adjuvant chemotherapy was given.

3. Discussion

Primary intrahepatic mesothelioma (PIHMM) is a very rare pathology. It is not included in the World Health Organization classification of hepatic tumors [4]. Mesothelioma is more common in men with a mean age of 58 years [5]. Histomorphologically, mesotheliomas are classified into two types: localized and diffuse. They can be further classified into three subtypes: predominantly epithelioid, sarcomatoid and biphasic types. Within the epithelioid category, they are arranged according to morphologic variations such as tubulopapillary and solid patterns.

The differential diagnosis includes several histological types of tumor; primary and secondary liver neoplasms, such as hepatocellular carcinoma, cholangiocellular carcinoma, and adenocarcinoma that had metastasized from an unknown site [6,7].

Mesothelial cells are not present in the liver under any normal condition. It might emerge from other types by transition. However, there is no evidence of transition yet. Some reported cases suggest that the primitive tumor may grow from the mesothelial cells of the Glisson's capsule, which eventually invade the liver [8].

A review of eleven cases is summed up in Table 1. The cases consisted of seven females and four males (2:1), with an age range of 50–83 years (median: 62 years). Only two patients (18.1%) had a history of asbestos exposure, disproving a previous study which showed that malignant mesothelioma is usually associated with asbestos exposure (86.8%) [9]. All eleven patients presented with localized tumor in the liver at the time of the initial diagnosis, and

Table 1
Characteristics of patients with PIHMM: PIHMM, Primary intrahepatic mesothelioma; F, Female; M, Male; Surg., Surgical; Lt., Left lobe; Rt., Right lobe; N/E, Not Evaluated; Sp., Spindle cells; Ep., Endothelial cells; Bp., Biphasic; BSC, Best Supportive Care; Tx., Treatment; LNR, *trans*-lymphatic Relapse; DI, Direct Invasion.

Author	Age	Sex	Asbestoses	Size(cm)	Type	Location	Tx.	Relapse	Follow-Up
Kottke-Marchan, 1989 [12]	83	F	N/E	15	Sp.	Lt.	Surg.	No	3 months
Di Blasi, 2004 [13]	61	F	N/E	10	Ep.	Rt.	Surg.	Yes	2 years
M. Buchholz, 2009 [11]	62	F	No	5.8	EP.	Rt. (S5, S8)	Surg.	LNR	20 months
Sakasi, 2009 [4]	66	M	Yes	4.4	Bp.	Rt.(S8)	Surg.	No	6 month
Gutgement, 2006 [1]	62	M	No	5.8	Ep.	Rt.	Surg.	LNR	5 months
Serter, 2014 [14]	56	F	No	15	Ep.	RT(S4, S7, S8)	Surg.	No	N/E
Serter, 2014 [14]	66	M	No	Multi	Bp.	Bilobated	Surg.	No	N/E
Inagaki, 2013 [15]	68	F	No	7	Ep.	Rt.(S7)	BSC	N/E	3 months
Lenonarda, 2003 [8]	54	F	Yes	12	Ep.	Rt.	Surg.	No	2 months
Dong, 2013 [16]	50	F	No	Multi	Ep.	Bilobated	Surg.	N/E	N/E
Kim, 2008 [17]	53	M	No	13	Bp.	Rt.	Surg.	DI	N/E
Present case	41	F	No	24	Bp.	Rt.(S5,S6,S7,S8)	Surg.	No	N/E

Table 2
Immunohistochemical phenotypes of PIHMM and conventional mesothelioma.

Author	Calretinin	CD2-40	CK5/6	CK7	CKAE1/3	WT-1	Vimentin	P53
Kottke-Marchan, 1989 [12]	N/E	N/E	N/E	N/E	N/E	N/E	+	N/E
Di Blasi, 2004 [13]	±	N/E	+	N/E	N/E	±	+	N/E
M. Buchholz, 2009 [11]	+	+	-	+	N/E	+	±	N/E
Sakasi, 2009 [4]	+	+	+	+	N/E	+	+	+
Gutgeman, 2006 [1]	+	+	-	+	N/E	+	±	+
Serter, 2014 [14]	+	N/E	N/E	N/E	N/E	N/E	N/E	N/E
Serter, 2014 [14]	+	N/E	+	N/E	N/E	N/E	+	N/E
Inagaki, 2013 [15]	+	±	N/E	+	N/E	+	+	+
Lenonarda, 2003 [8]	+	N/E	N/E	N/E	+	N/E	+	N/E
Dong, 2013 [16]	+	N/E	N/E	N/E	N/E	N/E	+	N/E
Kim, 2008 [17]	+	N/E	N/E	+	N/E	N/E	N/E	N/E
Present case	+	N/E	+	+	+	+	+	N/E

surgical removal was performed in all of the cases. However, four out of the ten patients who underwent surgical removal relapsed after surgery. Other authors reported a 55.1% metastasis-associated malignant mesothelioma at initial diagnosis [10].

Most of the cases reported had a tumor with a median size of 11.2 cm (range 4.4–15 cm). Our patient had the tumor double the size of all the reported cases, which was 21 cm in its largest dimension, making it the largest mesothelioma that has been reported. Furthermore, seven cases were of epithelioid type (63.6%), three were biphasic (27.3%) and one case was of sarcomatoid type (9.1%), while the prevalence of epithelioid, biphasic and sarcomatoid subtypes in a recent study was 32, 21.7 and 9.8% respectively [11]. The tumor immunohistochemistry of the reviewed cases are summarized in Table 2. We found the most dominant tumor marker to be Calretinin and Vimentin.

4. Conclusion

We present a very rare case of primary malignant mesothelioma of the liver found in a young female. Under microscope the mass showed epithelioid and spindled cells arranged in tri-structure pattern. Further investigation remains to be done on more cases of primary intrahepatic mesotheliomas to obtain morphology, prognosis and develop an appropriate treatment strategy for this rare tumor.

The work has been reported in line with the SCARE criteria [18].

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Conflicts of interest

The authors declared that there was no conflict of interest.

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Ethical Approval

This is a case report involving one patient and thus does not require IRB approval.

Author contribution

Ruba Haji Ali: writing the paper.
Mohamad Khalife: contributor.
Ghina El Nounou: data collection.
Ruba Zuhri Yafi: study design.
Hussein Nassar: data analysis.
Zeinab Aidibe: contributor.
Randa Raad: contributor.
Rania Abou Eid: contributor.
Walid Faraj: study concept.

Guarantor

Dr. Walid Faraj.

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